

Secondary adenocarcinoma of the urinary bladder attributed to metastatic gastroesophageal cancer

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Metastases of advanced gastrointestinal malignancy to the bladder is a rare phenomenon. Few such cases have

been reported. Here, we describe the case of a man with recurrent local gastroesophageal adenocarcinoma who presented with acute kidney injury and bilateral ureteral obstruction ultimately found to have de novo metastatic esophageal disease in the urinary bladder.

Key Words: gastroesophageal cancer, metastases, urinary bladder, malignant ureteral obstruction

Introduction

Approximately 81,500 new cases of urinary bladder cancer are diagnosed annually, and roughly 18,000 deaths are attributed to the disease.¹ Bladder cancer is more common in older white males and has a strong association with prior or current smoking history. Subtypes include urothelial carcinoma (most common, accounting for ~90% of bladder cancers), squamous carcinoma (accounting for 2%-7%), and adenocarcinoma (accounting for 0.5%-2%) amongst others.² While bladder cancers most commonly spread locally, distant metastatic sites include the lungs, pelvic bones, and liver. In rare circumstances, it has also been shown to metastasize to the skin, ovary, and muscle. The bladder

can also be seeded by cancers of other organs, including prostate,³ renal,⁴ breast,⁵ and lung cancers.⁶

Esophageal adenocarcinoma, on the other hand, comprises approximately 18,500 new diagnoses annually, with approximately 16,000 deaths.⁷ As with bladder cancer, tobacco use is a significant risk factor for the disease as well as alcohol use, age, male gender, concurrent gastroesophageal reflux disease, and the presence of precursor lesions like Barrett's esophagus. Given that systemic therapy is generally not curative, the mainstay of management is endoscopic or surgical resection. Interestingly, the general sites of metastasis include the surrounding lymph nodes, lungs, and bones, and until recently,^{8,9} there were no case reports of metastases to the urological organs. To our knowledge, this is the second reported case involving the bladder and the second known to have caused malignant ureteral obstruction.

Here, we discuss a patient with known gastroesophageal cancer recurrence who initially presented to the hospital with an acute kidney injury (AKI).

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Case report

The patient is a white man in his fifties with a past medical history of hypertension and benign prostatic hyperplasia (BPH) and ypT3N1 gastroesophageal adenocarcinoma status-post CROSS regimen (chemoradiotherapy prior to laparoscopic three-hole esophagectomy) and adjuvant FOLFOX. Twenty-three months after surgery and 18 months after adjuvant chemotherapy, he developed disease recurrence at the anastomosis and was no longer deemed a surgical candidate. He recently presented to our affiliated cancer hospital for evaluation prior to initiating salvage chemotherapy when he was incidentally found to have AKI, with a serum creatinine of 4.52 mg/dL (baseline = 0.69 mg/dL) and potassium of 4.4 mmol/L. After admission to the Oncology service, a renal-bladder ultrasound, Figure 1a, demonstrated moderate bilateral hydronephrosis, mild right hydroureter, a thickened bladder wall, and a 1.8 cm mass at the left ureterovesical junction. Urology was then consulted to assess the patient. Urinalysis was notable for 1+ blood, 1+ leukocyte esterase, pH of 6, specific gravity of 1.005, 2 RBCs/HPF, 4 WBCs/HPF, negative bacteria, and trace squamous cells.

On exam, the patient was comfortable and otherwise asymptomatic. He denied any fevers, nausea, vomiting, chills, flank pain, suprapubic pain, hematuria, and dysuria, but endorsed urgency and frequency over the past several months. The patient complained of nocturia two to three times nightly. He denied a sensation of

incomplete emptying. When questioned about his voiding history, the patient stated that he stopped taking tamsulosin years ago due to bothersome side effects. He was not initiated on an alternate therapy after tamsulosin cessation. The patient denied using tobacco, illicit drugs, or alcohol. He was in otherwise good physical condition. Digital rectal exam revealed a very firm, symmetric 30 cc gland without discrete masses. The patient's PSA was noted to be 1.39 ng/mL. Given the patient's history of untreated BPH, AKI, and bilateral hydronephrosis, Urology recommended the placement of a Foley catheter to facilitate upper tract decompression and intravenous hydration.

After approximately 15 hours of Foley decompression, the patient was noted to have a rapidly worsening renal function with a creatinine of 5.01 mg/dL and potassium of 5.1 mmol/L. Given his worsening kidney function and electrolyte derangement, the patient was expediently taken to the operating theatre for a cystourethroscopy, which not only demonstrated

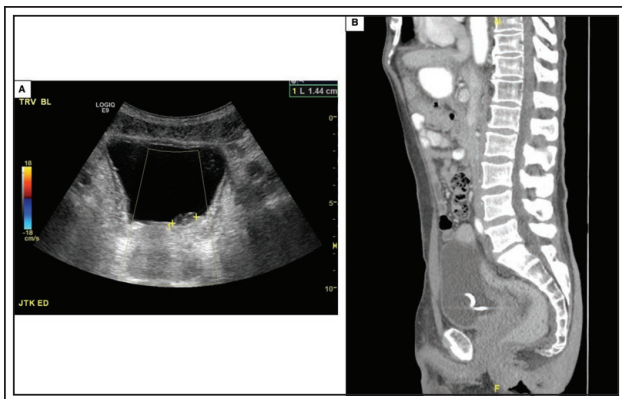


Figure 1. Pre and postoperative imaging. (A) Preoperative renal-bladder ultrasound (transverse plane) demonstrated the presence of a 1.8 cm bladder tumor (1.4 cm slice shown) overlying the left ureterovesical junction. (B) Postoperative CT of the abdomen and pelvis (sagittal plane) showed an enlarged prostate and diffuse soft tissue along the posterior bladder wall and sides bilaterally.

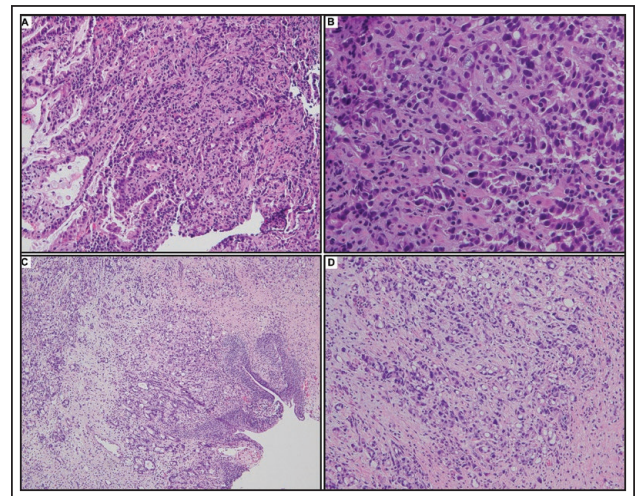


Figure 2. Histologic analysis of TURBT specimens. (A) High power (20x) hematoxylin and eosin (H&E) image of a poorly differentiated esophageal adenocarcinoma involving corpus-type mucosa at the G-E junction. Immunohistochemistry (IHC) for HER2/neu was negative. (B) High power (40x) H&E image showing infiltrating single cells with focal signet-ring cell features. (C) Medium power (10x) H&E image of esophageal adenocarcinoma involving the urinary bladder. Benign overlying urothelium is seen with underlying carcinoma. IHC demonstrated positive staining for CK7 and focally for CDX2, while negative stains included GATA3, P63, and NKX3.1. (D) High power (20x) H&E image demonstrating infiltrating single cells with signet-ring cell morphology, resembling the primary tumor.

mildly occlusive bilobar prostatic hypertrophy, but also a 5 cm papillary bladder mass encompassing the bladder base and trigone. Neither ureteral orifice (UO) could be visualized. Transurethral resection (TURBT) was performed over the area of both UOs to reveal the orifices themselves, and bilateral indwelling J-J 8-French ureteral stents were placed over wires. An impressive burden of disease can be visualized in the CT scan (sagittal view) in Figure 1b.

Bladder urine cytology demonstrated rare atypical cells. The TURBT histology demonstrated a poorly differentiated adenocarcinoma with glandular and signet-ring cell morphology, resembling the primary tumor, Figure 2. While lesional cells were positive for CK7, supporting either an upper gastrointestinal origin or a bladder primary, negative GATA3 and p63 immunostaining argued against urothelial carcinoma. Focal CDX2 positivity, a marker of gastrointestinal origin, supported an esophageal carcinoma metastasis in the clinical context. NKX3.1, which was negative, was also assessed to exclude a prostatic primary via local infiltration.

Postoperatively, the patient was managed with a 20Fr three-way hematuria Coude Foley catheter and continuous bladder irrigation, which was clamped and discontinued on postoperative day (POD) 1. His postoperative creatinine initially spiked to 5.14 mg/dL before gradually down-trending to 2.05 mg/dL on POD4. The patient's hyperkalemia followed a similar trajectory. He was discharged uneventfully on POD4 with plans to follow up with Urology for ureteral stent exchanges on a quarterly basis and with Oncology for management of metastatic esophageal disease. The Foley catheter was removed on the day of discharge. The patient's creatinine ultimately nadired at 1.57 mg/dL on POD11.

Discussion

Metastatic primary bladder cancer has been shown to spread to contiguous urological organs (i.e., prostate and kidney), organs of close proximity (colon), and more distantly the lung, ovary, and bones. Upper gastrointestinal malignancy metastasis has customarily progressed to the surrounding lymph nodes, lungs, and bone.¹⁰ Here, we describe a rare instance in which a recurrent gastroesophageal adenocarcinoma metastasized to the urinary bladder and caused bilateral malignant ureteral obstruction.

What makes this case particularly interesting is that the patient denied the classic presenting symptom of a bladder cancer (hematuria) nor did he have the classic social risk factors (smoking, industrial chemical exposures, diabetic with prior history of pioglitazone

use, "nutraceutical" use, or arsenic exposure). He did have other concerning symptoms, such as fatigue, anorexia and weight loss, and early satiety that were concomitant with his known GE adenocarcinoma recurrence. In the setting of this recurrence, the patient delayed seeking further urologic evaluation of his BPH.

Per AUA guidelines, the typical work up for an incidental bladder mass or hematuria involves comprehensive cystoscopic evaluation, as complete as possible a resection of the suspected lesion(s), and full upper tract imaging. Here, given the unknown identity of the mass, appearance of an adenocarcinoma, and location of the lesion (at the bladder neck, with anatomically close proximity to the rectum), a complete resection was purposefully avoided until pathologic analysis was completed. At present, the patient is slated to begin salvage chemotherapy with FOLFOX.

Conclusion

Bladder manifestations of metastatic gastrointestinal disease are exceedingly rare. At least two other cases have been described to date. While tumors of the bladder can take on a variety of appearances, pathologic diagnosis via TURBT remains the gold standard for diagnosing tumor type and guiding treatment options. □

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